



General

Guideline Title

Ranibizumab for treating choroidal neovascularisation associated with pathological myopia.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Nov. 41 p. (Technology appraisal guidance; no. 298).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Ranibizumab is recommended as an option for treating visual impairment due to choroidal neovascularisation secondary to pathological myopia when the manufacturer provides ranibizumab with the discount agreed in the patient access scheme.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Choroidal neovascularisation associated with pathological myopia

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Family Practice

Ophthalmology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of ranibizumab for treating choroidal neovascularisation associated with pathological myopia

Target Population

Adults with visual impairment due to choroidal neovascularisation associated with pathological myopia

Interventions and Practices Considered

Ranibizumab

Major Outcomes Considered

- Clinical effectiveness
 - Best corrected visual acuity in the studied eye
 - Adverse effects of treatment
 - Health related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Aberdeen Health Technology Assessment (HTA) Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description of Manufacturer's Search Strategies and Critique

The manufacturer searched an appropriate range of databases that included MEDLINE, EMBASE, Science Citation Index, the Cochrane Library and the major international trials registries. The websites of some Health Technology Assessment and Regulatory Agencies and recent conference proceedings of the major professional ophthalmology organisations were also searched. Searches were initially undertaken in March 2012 and updated in November 2012. The search strategies used for each database are detailed in the manufacturer's submission and were reproducible. The approach adopted by the manufacturer was to search for any publication concerning choroidal neovascularisation (CNV) associated with myopia. No terms relating to the intervention, comparators or study design were included in the strategy. The facets of the search (CNV and myopia) were correctly constructed using both appropriate text and controlled vocabulary terms and were combined using the correct Boolean operators. By adopting this approach, it is likely that the literature search was highly sensitive.

Because these searches were disease-specific without further restriction by intervention or study design, no additional searches were undertaken for the indirect comparisons or adverse events. This seems entirely appropriate.

Inclusion Criteria

Table. Inclusion Criteria for Systematic Review of Clinical Effectiveness

Population	Patients of any age undergoing treatment for choroidal neovascularisation (CNV) secondary to pathological myopia (PM), including patients with concomitant ocular disease
Intervention	Any types of treatment for CNV, including (but not restricted to) thermal laser photocoagulation therapy, surgery, verteporfin photodynamic therapy (vPDT) and anti-vascular endothelial growth factor (VEGF) therapy (e.g., bevacizumab and ranibizumab)
Comparator	'Standard care' defined as vPDT or laser treatment and other treatments identified in randomised controlled trials (RCTs) were eligible for inclusion
Outcomes	Visual acuity (ETDRS letters or logMAR); other measures of visual acuity such as blindness and lack of response; structural changes (e.g. foveal thickness and central retinal thickness), health-related quality of life (HRQoL), ocular and systemic adverse events (AEs)
Study Design	RCTs of any duration; cross-over RCTs if data were presented at the time of cross-over; prospective randomised studies; open-label extension studies of RCTs; case series of ≥ 25 patients for ≥ 6 months
Language Restriction	None

The ERG undertook an independent literature search. This was more focused, primarily to identify any relevant RCTs, and was carried out on a restricted range of databases: MEDLINE, MEDLINE In-Process, EMBASE and CENTRAL. These searches were performed in June 2013 and so will have captured additional studies which had been added to the databases after the manufacturer's search in November 2012. The searches are detailed in Appendix 1 of the ERG report (see the "Availability of Companion Documents" field).

Cost-effectiveness

Description of Manufacturer's Search Strategies and Critique

The disease-specific searches undertaken for the clinical effectiveness review were used to identify the cost-effectiveness studies. As well as the clinical databases, the appropriate health economic sources were searched and included EconLit and National Health Service Economic Evaluation Database (NHS EED). The manufacturer undertook additional, less focussed searches of MEDLINE and EMBASE for any economic

evaluations associated with degenerative or pathological myopia without reference to CNV. The facets for the search (myopia and economic evaluation) were correctly constructed, using the relevant text and controlled vocabulary terms, and were combined correctly with Boolean operators. Reference lists of eligible studies and recent reviews were checked for additional studies. This overall approach was considered by the ERG to be robust and likely to have retrieved the relevant articles.

Inclusion and Exclusion Criteria

Economic evaluations of patients undergoing any treatment for PM or CNV secondary to PM (including patients refractory to other therapies) were eligible for inclusion. Relevant outcomes included total, direct and indirect costs, summary health outcomes, utility values, cost-effectiveness ratios and number of cases of blindness.

Number of Source Documents

Clinical Effectiveness

Three randomised controlled trials and six non-randomised studies were included by the manufacturer.

Cost-effectiveness

- One published cost-utility study was included.
- The manufacturer submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Aberdeen Health Technology Assessment (HTA) Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Quality Assessment

The manufacturer assessed the quality of the three included randomised controlled trials (RCTs). The methods used for quality assessment were considered adequate by the ERG.

Overall, the methodological quality of the Novartis phase III trial was acceptable. Both the methods of randomisation and the treatment allocation concealment were adequate. Randomisation appears to have been successful and demographic and choroidal neovascularisation (CNV) characteristics were balanced across the randomised groups. Study personnel and participants were masked throughout the trial. The only study personnel who were unmasked were those who administered the randomised study treatment when needed, according to the protocol. All outcomes were assessed by masked personnel. The ERG considers the masking strategies used to be appropriate. Analysis was on an intention-

to-treat basis. The full analysis set involved a modified last-observation-carried-forward (LOCF) approach. The ERG considers this approach to be acceptable in this case.

The quality of the Gharbiya 2010 trial was unclear due to inadequate reporting. Method of randomisation, concealment of treatment allocation and details of any masking were not reported, although it appears that no masking was involved in the trial. Methods of analysis were also not reported, thus it is unclear whether an intention-to-treat approach was used.

The quality of the Iacono 2012 trial was variable. Appropriate randomisation and concealment of treatment allocation procedures were involved. Baseline disease-related characteristics were comparable across treatment groups. The trial was described as "double-blind" but only masking of the study personnel administering the injection was declared. Thus, it is unclear whether masking of participants was achieved. An intention-to-treat approach was used but methods of accounting for missing data were not described.

The ERG performed a quality assessment of the manufacturer's systematic review using the York Centre for Reviews and Dissemination (CRD) criteria (see Table 6 in the ERG report [see the "Availability of Companion Documents" field]). The quality of the systematic review was good and the ERG has no major concerns in any of the quality areas.

Critique of Indirect and Mixed Treatment Comparisons

The manufacturer did not present an indirect comparison of ranibizumab with other treatments. Their reason was that there was a head to head trial of ranibizumab versus verteporfin photodynamic therapy (vPDT), the only comparator considered in the submission. As bevacizumab was not included as a comparator they felt it unnecessary to undertake a network meta-analysis. The manufacturer did present a preliminary network analysis including a number of treatments (observation, vPDT, ranibizumab, bevacizumab, laser). However, following clarification, they confirmed it was inappropriate given the heterogeneous nature of the study populations and the differing length of follow ups. Therefore, within the main submission, a network meta-analysis of ranibizumab with treatments other than vPDT was not presented.

See section 4 of the ERG report (see the "Availability of Companion Documents" field) for more information on clinical effectiveness.

Cost-effectiveness

Model Structure

The manufacturer developed a cost utility Markov model with a quarterly cycle and a lifetime horizon. It is principally a one eye model, though some additional costs are included for bilateral disease at baseline. The distribution of the visual acuity of the treated eyes is divided into eight health states, the majority of which span a range of 10 ETDRS letters. The baseline distribution and proportions that have their baseline best seeing eye (BSE) treated are drawn from the Novartis phase III trial.

See section 5 of the ERG report (see the "Availability of Companion Documents" field) for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee considered the manufacturer's economic model and the critique and exploratory analyses performed by the Evidence Review Group (ERG). It accepted the model structure, but was concerned by some of the uncertainties about the assumptions used by the manufacturer. The Committee noted that the manufacturer had not included bevacizumab as a comparator in its economic model.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee considered the larger proportion of patients with subfoveal involvement in the Verteporfin in Photodynamic Therapy (VIP) trial, which provided the verteporfin photodynamic therapy (vPDT) data after 3 months. However, it concluded that the imbalance between RADIANCE and VIP was unlikely to have a large impact on the manufacturer's model.

The Committee considered the manufacturer's assumption that the average best corrected visual acuity (BCVA) gain at the end of year 1 would continue indefinitely. It concluded that the duration of treatment benefit was likely to be less than the manufacturer's assumption of an indefinite duration, but that ranibizumab dominated vPDT when the duration of effect was reduced.

The Committee discussed whether the manufacturer's assumption about the number of ranibizumab injections that people would receive in clinical practice was too low. It concluded that the number of injections included in the manufacturer's base case could be an underestimate, and that even if the number of injections was increased, the base-case analysis would not be affected.

The Committee discussed whether the costs of blindness used in the manufacturer's model were too high. The Committee noted that the ERG presented lower costs of blindness in their report. The Committee concluded that the ERG's assumptions about the costs of blindness were likely to be more realistic than those used by the manufacturer, and that any changes were unlikely to have a large impact on the base-case analysis.

The Committee discussed whether the administration costs of ranibizumab used in the manufacturer's model were an underestimate. It concluded that the National Health Service (NHS) costs were uncertain, but the uncertainty was not great enough to affect the base-case analysis.

The Committee discussed whether the mortality multipliers used in the manufacturer's economic model were appropriate. It concluded that the manufacturer's rationale for some of the mortality multipliers in the model was unclear, and that any changes to them were unlikely to change the

base-case analysis.

The Committee discussed whether the method used in the manufacturer's model to account for the possibility of the treated eye changing from being the better-seeing eye to the worse-seeing eye as patients change health states was appropriate. It concluded that the modelling may have had an impact on the base-case analysis, but the level of impact was unclear.

The Committee considered that Euroqol 5 dimensions (EQ-5D) data were collected in RADIANCE, but were not used in the manufacturer's economic model. It concluded that using the EQ-5D data from RADIANCE was unlikely to change the overall results of the base-case analysis.

Incorporation of Health-Related Quality-of-Life Benefits and Utility Values

The Committee noted that the EQ-5D data collected in RADIANCE was not used in the model and the manufacturer used utility values from Czoski-Murray et al. (2009), in line with previous appraisals of drugs for eye conditions. The Committee heard from the ERG that using the EQ-5D data from RADIANCE did not have had a large effect on the model, although the effect for the worse-seeing eye was not clear. The Committee concluded that using the EQ-5D data from RADIANCE was unlikely to change the overall results of the base-case analysis.

Have Any Potential Significant and Substantial Health-Related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee was not aware of any substantial benefits of ranibizumab over its comparators that were not already captured in the quality-adjusted life year (QALY) estimation in the modelling.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost-Effective?

None

What Are the Key Drivers of Cost-Effectiveness?

The manufacturer's sensitivity analyses showed that the cost-effectiveness of ranibizumab was sensitive to changes in the unit cost of ranibizumab and vPDT, the number of ranibizumab injections in the first and second year, the starting age of the patient group, the discount rate for benefits, and the maximum utility gain in the worse-seeing eye.

Most Likely Cost-Effectiveness Estimate (given as an incremental cost-effectiveness ratio [ICER])

The Committee noted that manufacturer's base-case analysis showed that ranibizumab dominated vPDT (that is, it was more effective and less costly), resulting in more QALYs (13.18 compared with 12.75) and lower costs (£9694 compared with £12,455). The Committee considered the uncertainties in the manufacturer's model and noted that they were unlikely to have an effect on the overall results of the base-case analysis, which showed that ranibizumab dominated vPDT.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report, and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of ranibizumab and a review of this submission by the Evidence Review Group. For clinical effectiveness, three randomised controlled trials were the main source of evidence. For cost-effectiveness, the manufacturer's economic model was considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of ranibizumab for treating choroidal neovascularisation associated with pathological myopia

Potential Harms

Adverse reactions to treatment are mostly limited to the eye. Those commonly reported in clinical trials include vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival haemorrhage, eye irritation, sensation of a foreign body in the eye, increased production of tears, blepharitis, dry eye, ocular hyperaemia, itching of the eye and increased intraocular pressure. Nasopharyngitis, arthralgia and headaches are also commonly reported.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Contraindications

Contraindications

Contraindications to ranibizumab include known hypersensitivity to the active substance or to any of its excipients, active or suspected ocular or periocular infections, and active severe intraocular inflammation.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Clinical Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Service (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a patient has choroidal neovascularisation associated with pathological myopia and the doctor responsible for their care thinks that ranibizumab is the right treatment, it should be available for use, in line with NICE's recommendations.
- The Department of Health and the manufacturer have agreed that ranibizumab will be available to the NHS with a patient access scheme which makes ranibizumab available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the manufacturer to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to the manufacturer.
- NICE has developed a costing statement to help organisations put this guidance into practice, which is available on the [NICE Web site](#) (see also the "Availability of Companion Documents" field).

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Nov. 41 p. (Technology appraisal guidance; no. 298).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Nov

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Professor Andrew Stevens (*Chair of Appraisal Committee C*), Professor of Public Health, University of Birmingham; Professor Kathryn Abel, Director of Centre for Women's Mental Health, University of Manchester; Dr David Black, Medical Director, NHS South Yorkshire and Bassetlaw; David Chandler, Lay Member; Gail Coster, Advanced Practice Sonographer, Mid Yorkshire Hospitals NHS Trust; Professor Peter Crome, Honorary Professor, Department of Primary Care and Population Health, University College London; Dr Maria Dyban, General Practitioner, Kings Road Surgery, Cardiff; Professor Rachel A Elliott, Lord Trent Professor of Medicines and Health, University of Nottingham; Dr Greg Fell, Consultant in Public Health, Bradford Metropolitan Borough Council; Dr Wasim Hanif, Consultant Physician and Honorary Senior Lecturer, University Hospital Birmingham; Dr Alan Haycox, Reader in Health Economics, University of Liverpool Management School; Dr Peter Jackson, Clinical Pharmacologist, University of Sheffield; Dr Janice Kohler, Senior Lecturer and Consultant in Paediatric Oncology, Southampton University Hospital Trust; Emily Lam, Lay Member; Dr Allyson Lipp, Principal Lecturer, University of South Wales; Dr Claire McKenna, Research Fellow in Health Economics, University of York; Professor Gary McVeigh, Professor of Cardiovascular Medicine, Queens University Belfast and Consultant Physician, Belfast City Hospital; Dr Grant MacLaine, Formerly Director, Health Economics and Outcomes Research, BD, Oxford; Dr Andrea Manca, Health Economist and Senior Research Fellow, University of York; Henry Marsh, Consultant Neurosurgeon, St George's Hospital, London; Dr Paul Miller, Director, Payer Evidence, AstraZeneca UK Ltd; Dr Anna O'Neill, Deputy Head of Nursing and Healthcare School/Senior Clinical University Teacher, University of Glasgow; Alan Rigby, Academic Reader, University of Hull; Professor Peter Selby, Consultant Physician, Central Manchester University Hospitals NHS Foundation Trust; Dr Paul Tappenden, Reader in Health Economic Modelling, School of Health and Related Research, University of Sheffield; Dr Judith Wardle, Lay Member

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .

Availability of Companion Documents

The following are available:

- Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Nov. 6 p. (Technology appraisal 298). Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) .
- Cummins E, Fielding S, Cruickshank M, Fraser C, Lois N, Brazzelli M. Ranibizumab for the treatment of choroidal neovascularisation associated with pathological myopia. Aberdeen (Scotland): Aberdeen HTA Group, Institute of Applied Health Sciences, University of Aberdeen; 2013. 139 p. Electronic copies: Available from the [NICE Web site](#) .

Patient Resources

The following is available:

- Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Nov. (Technology appraisal 298). Electronic copies: Available from the [National Institute for Health and Care Excellence \(NICE\) Web site](#) . Also available for download as a Kindle or EPUB ebook from the [NICE Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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